POSSIBLE ROLE OF METHYLATED PHOSPHALIPIDS IN PARKINSONISM, CAUSED BY EXCESS S-ADENOSYL-L-METHIONINE-INDUCED METHYLATION.

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The CNS injection of S-adenosyl-methionine (SAM) causes tremors, rigidity, hypokinesia, the depletion of dopamine (DA), L-DOPA and tyrosine hydroxylase (TH) as well as substantia nigra (SN) neuronal degeneration; changes that resemble the symptoms of Parkinson's disease (PD). The motor effects of SAM may be due to the depletion of DA and L-DOPA, TH-depletion may be due to SN degeneration, but the mechanism by which the SN neurons were damaged is unknown. In the CNS the methylation of phosphatidylethanolamine (PTE) by SAM produces phosphatidylcholine (PTC) and PTC produces lyso-PTE, a potent lysolytic and cytotoxic surfactant, that damages cell membranes and fibers, reduces DA receptor binding and is involved in ischemic cell death; so lyso-PTC may play a role in SAM-induced SN damage. To know this, lyso-PTC was injected into the brain of rats. The injection of lyso-PTC into the lateral ventricle caused tremor, teeth chattering, hypokinesia, and erosion and dilation of the ventricles. Following injection of SAM into the caudate nucleus (CN), denuded neurons, gliosis, axonal swelling and filamentous remains of blood microvessels were seen proximal to the injection site. Myelin staining traced degeneration, retrogradely, to the SN. In the SN Nissl staining showed degenerated neurons and silver staining identified axonal stumps. These findings show that phosphalipids (PL), which represent about 19% of dry cell mass, may play a role in SAM-induced parkinsonism and SN damage. In addition, the blood microvessels damage caused by lyso-PTC suggests that lyso-PTC could be involved in other CNS damage, like cerebrovascular accidents; noting that high levels of PTE, PTC and lyso-PTC, are found in blood vessels and plasma. Lyso-PTC may also serve as a neuronal tracer. Supported by NIH RR 03020 and RO1 28432 and 31177.